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EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,366	HOLM, PER SONNE	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-178* is/are pending in the application.

4a) Of the above claim(s) *150-177* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89-122,124-128,134-142 and 178* is/are rejected.

7)☒ Claim(s) *123,129-133 and 143-149* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/25/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Election/Restriction

Applicant's election without traverse of Group I, Claims 89-149 and 178, in the reply filed on 11/29/07 is acknowledged.

Claims 150-177 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/29/07.

Specification

A substitute specification excluding the claims is required pursuant to 37 CFR 1.125(a) because: A substitute specification in proper idiomatic English and in compliance with 37 CFR 1.52(a) and (b) is required. The as filed specification is replete with grammatical errors and a substitute specification is required.

A substitute specification must not contain new matter. The substitute specification must be submitted with markings showing all the changes relative to the immediate prior version of the specification of record. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived. An accompanying clean version (without markings) and a statement that the substitute specification

contains no new matter must also be supplied. Numbering the paragraphs of the specification of record is not considered a change that must be shown.

Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Sequences are present in the specification which have not been identified by the appropriate SEQ ID NO identifiers. The nature of the non-compliance has not however, precluded an examination of the application on the merits, the results of which are communicated below.

Improper Multiple Dependent Claims

Claims 143-149 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must depend from other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims 143-149 have not been further treated on the merits.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

35 USC 101 Rejections

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 89-93, 112-117, 120, 124, 135-136 and 138-142 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Applicants claim, in claims 89-93, an adenovirus, which can be a naturally occurring adenovirus, wherein any first protein is expressed prior to any second protein. The limitations of the first protein being a E1B and/or E4 protein and the second being an E1A are not limiting because the claims use improper open Markush language ("selected from the group **comprising** (emphasis added)" to recite the alternatives. It is noted that use of the **open** legal transitional phrase "comprising" is improper in a Markush claim (See MPEP 2173.05(h)). In claims reciting that the first protein is specifically E1B or E4, the second protein in not limited to any specific adenoviral protein and can be for example, any of the later adenoviral proteins, i.e. L1-L5, etc. Use of the term "comprising" in the instant claims in a Markush format means that the Markush group is open to any and all proteins, not just the recited adenoviral proteins. The claims reciting mutated adenoviruses wherein the E1, E3 or E4 regions are inactive read on naturally occurring adenovirus mutants. Claims reciting adenoviruses with certain expression cassettes likewise reads on naturally occurring adenoviruses

because the "expression cassettes" read on naturally occurring adenoviral promoter – polypeptide coding region expression cassettes. With regard to the adenovirus being capable of replicating in cells containing YB-1 in the nucleus independent of the cell cycle, it is noted that the claims read on naturally occurring adenoviruses which would be capable of replicating in cells with the recited YB-1 activity as this protein would not interfere with normal adenoviral replication. With regard to the claimed replication system, this reads on normal adenovirus replication and gene expression in infected cells, i.e. the system comprises a infected cell comprising an adenoviral nucleic acid which can have a naturally occurring mutation in an E1A or E1B or E4, etc. region and additional adenoviral nucleic acids which lack this mutation and can have a helper function with regard to the missing gene activity. The cells of claims 147-149 likewise read on cells naturally infected with adenoviruses. The rejected claims therefore read on products of nature, which is non-statutory subject matter.

Additionally, the cells recited in claims 147-149 read on cells which can be in a human because the adenoviruses and adenovirus vectors are contemplated for treatment of disease in humans. Since the cell is intended to be present in a human being, the cell will be integrated into the human being and therefore become an inseparable part of the human being. The scope of the claims therefore encompasses a human being, which is non-statutory subject matter. Redrafting the claims to recite an isolated cell or cell *in vitro* would be remedial to distinguish the claims from embodiments encompassing a human being.

35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 89-105, 109-115, 117-122, 124-126, 134-142 and 178 are rejected under 35 U.S.C. 102(b) as being anticipated by Hallenbeck et al. (US 5,998,205).

Applicants claim an adenovirus expressing a first protein which is selected from the group comprising an E1B protein and an E4 protein, prior to a second protein which is selected from the group comprising an EIA-protein. Applicants also claim adenoviruses which comprise the E1A, E1B or E4 genes under control of a heterologous promoter or functionally inactive E1A, E1B or E4 genes. Applicants also claim adenoviruses which provide YB-1 in the nucleus through at least one adenoviral protein or that the provision of YB-1 in the nucleus is mediated through at least one adenoviral protein, whereby preferably the adenoviral protein is different from EIA.

The examiner is interpreting the claims as noted in the above 101 rejection.

Hallenbeck et al. (See whole document, particularly Claims 1-20, columns 5-8, 10, etc.) teaches adenoviruses which comprise the E1B and/or E1B or E4 coding regions under control of heterologous promoters (can be tissue specific or tumor specific, etc.) and optionally comprising expression cassettes for expression of antisense or ribozyme sequences and apoptosis inducing genes (i.e. E1A or E4). With regard to the limitation that the claimed adenovirus provides YB-1 in the nucleus

through at least one adenoviral protein, it is noted that the adenoviral protein E1B-55k normally targets the YB-1 protein to the nucleus and this is an inherent property of the natural E1B-55k protein (See Holm et al., Journal of Biological Chemistry, March 2002, Vol. 277, No. 12, pp. 10427-10434) which would be present in the adenoviruses recited by Hallenbeck et al. and said YB-1 and E1B-55k normally act jointly to facilitate adenovirus replication. With regard to claim limitations reciting that the E1, E3 or E4 regions are functionally inactive, Hallenbeck et al. teach functionally inactive E1 and E4 regions wherein the E1 or E4 coding regions are operably linked to promoters (i.e. tumor specific promoters) which are inactive in normal cells, rendering the genes functionally inactive in normal cells. The adenoviruses disclosed by Hallenbeck et al. can be classified as recombinant and/or mutant as they have modifications to the genome. Hallenbeck et al. therefore teaches the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 127-128 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Irving et al. (US 20030095989).

Applicants claim an adenovirus comprising a nucleic acid encoding YB-1 under control of a promoter.

Irving et al. (published 5/22/2003, filed 12/17/2001, see whole document, particularly paragraph [0105]) recites generation of a adenoviral vector comprising the YB-1 encoding region under control of the CMV promoter/enhancer. Irving et al. therefore teaches the claimed invention.

Applicant cannot rely upon the foreign priority papers to overcome this rejection under 35 USC 102(a) because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Statutory Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 89-91 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-3 of copending Application No. 10/579,543. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 4-58 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 92-142 and 178 of copending Application No. 10/579,543 (hereafter the '543 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite the same adenoviruses, vectors and expression systems. The claims in the '543 application differ from those in the instant application only in that they are improperly multiply dependent and hence each reads on a broader scope. However, the claims in the '543 application, if drafted properly, would read on the instant invention and indeed, each of the claims in the '543 application comprises an

alternative embodiment which would anticipate each of the instant claims. The claims are therefore obvious one over the other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 127-128 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47-48, 59-60, 65 of copending Application No. 10/451,210 (hereafter the '210 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite an adenovirus comprising a nucleic acid sequence encoding YB-1. The instant claim 128 recites that the YB-1 sequence is under control of a promoter while the '210 claims do not explicitly recite a promoter for this sequence. However, it would have been obvious for the ordinary skilled artisan to operably link a promoter to the YB-1 coding sequence because expression of the YB-1 sequence is essential for operation of the adenoviral replication system recited in the '210 claims. If the YB-1 protein is not expressed, it makes no sense to include a nucleic acid sequence encoding it in the adenoviral vector. The claims are therefore obvious one over the other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

35 USC 112, 2nd Paragraphs

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 94-108 and 112-116 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 94 (and dependent claims) are vague in that applicants recite "the at least one protein is under control of a promoter". A protein cannot be under control of a promoter; however, **a nucleic acid sequence encoding a protein** can be under control of a promoter.

Claim 112, (and dependent claims) are vague in that claim 112 recites that the adenovirus comprises at least one functionally inactive adenoviral region, whereby the region is selected from the group comprising the E1 region, the E3 region, the E4 region and combinations thereof, while the claims depends from claim 89 which recites that the adenovirus can express E1B or E4 prior to expressing E1A. It is unclear how the **same genes which are recited as being expressed in claim 89 are then functionally inactive in claim 112**.

Claim Objections

Claims 123 and 129-133 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D., can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo
February 8, 2008